REMARKS

Claims 4, 6, 9-14, 44 and 45 were pending in this application before entry of the amendments made herein.

Claim 4 has been amended for purposes of clarity. In particular, claim 4 has been amended to recite that the ErbB-3 protein is a fragment of the extracellular domain of ErbB3 and is not the entire extracellular domain of ErbB3. Claim 4 also has been amended to correct a minor editorial error. Support for the amendments can be found in the specification as originally filed at, *inter alia*, page 12, last paragraph, lines 1-3; and page 13, second paragraph.

No new matter has been added by these amendments. Upon entry of the present amendment, claims 4, 6, 9-14, 44 and 45 will be pending in the present application.

I. THE CLAIM REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, SHOULD BE WITHDRAWN

Claims 4, 6, 9-14, 44 and 45 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Specifically, the Examiner alleges that "the specification does not provide an adequate written description of extracellular domains of ErbB-3 or ErbB-3 proteins comprising amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14, wherein the ErbB-3 proteins are not the extracellular domain of ErbB3 that function to generate an immune response and prevent, treat or delay a neoplasm" that is required to practice the claimed invention (see Office Action, page 9, last paragraph, lines 1-6).

Although Applicant disagrees, solely to expedite prosecution of this application, Applicant has amended independent claim 4 for purposes of clarity. As amended, claim 4 recites that the ErbB-3 protein is a fragment of the extracellular domain of ErbB3 and comprises (a) the amino acid sequence set forth in SEQ ID NO: 3; or (b) amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14; or (c) amino acid residues 2-139 of the amino acid sequence set forth in SEQ ID NO:16, and is not the entire extracellular domain of ErbB3.

Applicant submits that the specification provides adequate written description of the subject matter recited in amended claim 4. For example, the specification (see page 12, second paragraph) discloses a method for preventing, treating or delaying neoplasm in a mammal, which method comprises administering to a mammal, to which such prevention,

treatment or delay is needed or desirable, an effective amount of an ErbB-3 protein, whereby an immune response is generated against said neoplasm and said neoplasm is prevented, treated or delayed. The specification (see page 12, last paragraph, lines 1-3) also discloses that any suitable ErbB-3 protein that can elicit an immune response to the neoplasm to be prevented, treated or delayed, can be used in the method. In addition, the specification (see page 13, lines 3-5) describes that "[i]n a preferred embodiment, an effective amount of an extracellular domain of an ErbB-3 protein, or *a functional fragment thereof*...is administered" (emphasis added). Moreover, the specification (see page 13, second paragraph) describes that such a fragment can comprise (a) the amino acid sequence set forth in SEQ ID NO: 3; or (b) amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14; or (c) amino acid residues 2-139 of the amino acid sequence set forth in SEQ ID NO:16.

Applicant submits that the term "extracellular domain" is well known to one skilled in the art, such that one skilled in the art would understand that the phrase "extracellular domain of ErbB3" means the region of ErbB3 which is located outside of the cell membrane. One skilled in the art also would understand that the phrase "a fragment of the extracellular domain of ErbB3" means a portion of the region of ErbB3 which is located outside of the cell membrane.

The Examiner alleges that "the specification repeatedly discloses proteins or nucleic acids encoding 'an extracellular domain of the ErbB-3 protein' and discloses plural forms of extracellular domains, indicating there is more than one extracellular domain in the invention" (see Office Action, page 4, lines 4-7) (original emphasis). The Examiner further alleges that "[t]he art teaches various extracellular domains of ErbB-3," for example, "Lee et al...teach the extracellular domain is the amino terminal residues 1-620 (Figure 1)" and "Krause et al...teach the extracellular domain or ErbB-3 is amino acids 20-643 of Figure 3)" (see Office Action, page 4, second paragraph, lines 1-4).

In response, Applicant submits that one skilled in the art would understand that ErbB3 only has one extracellular domain. The Examiner's attention is respectfully directed to the following references which define the various domains of ErbB3:

	Extracellular	Transmembrane	Cytoplasmic
Plowman et al.[1]	1-612 (1-631)	613-645 (632-664)	646-1323 (665-1342)
Lee et al.[2]	1-620 (1-639)	621-646 (640-665)	647-1323 (666-1342)
Kraus et al.[3]	1-643	644-664	665-1342

Note: the numbers in the brackets reflect inclusion of the 19-aa signal sequence.

There are minor differences between these references of the exact region of the extracellular domain of ErbB3. However, one skilled in the art would expect such differences, since the structural partition of the protein was estimated based on general characteristics of the amino acids, and could vary by assumptions undertaken by investigators. For example, Plowman et al. and Lee et al. did not include the signal sequence in the extracellular domain of ErbB3, whereas Kraus et al. and the inventor of the instant application included the signal sequence in the extracellular domain of ErbB3. As disclosed in the specification, the extracellular domain of ErbB3 is 1-640 (SEQ ID NO:2), including the signal sequence. SEQ ID NO:3, which is 190 amino acids long, is a functional fragment of the extracellular domain of ErbB3.

In the Office Action (see page 4, lines 7-10), the Examiner alleges that while it appears that rhErbB3-f12 (i.e., SEQ ID NO:14) reduced tumor growth in inoculated mice compared to controls, the type of cancer the mice developed is unclear according to Table 4 at page 30 of the specification. Applicant submits that the specification discloses that the tumor model used to test the anti-tumor effects of rhErbB3-f12 was established through the transplant of tumor cell from FVB/N transgenic mice (from The Jackson Laboratory) to the site under the breast of another tumor-free mice (see page 26, first and second paragraphs; and page 27, lines 3-5). One skilled in the art would understand that a FVB/N transgenic

[1] Plowman et al., "Molecular cloning and expression of an additional epidermal growth factor receptor-related gene," PNAS, 1990, 87:4905-4909, copy made of record as reference C34 in the Information Disclosure Statement filed March 2, 2009. See page 4906, right column, second entitled "Structural Domains of HER3," first and second paragraph; and Figure 1 at page 4907.

[2] Lee et al., "A naturally occurring secreted human ErbB3 receptor isoform inhibits heregulin-stimulated activation of ErbB2, ErbB3, and ErbB4," Cancer Research, 2001, 61:4467-4473, copy made of record as reference C29 in the Information Disclosure Statement filed March 2, 2009. See Figure 1 at page 4468.

[3] Kraus et al., "Isolation and characterization of ERBB3, a third member of the *ERBB*/epidermal growth factor receptor family: Evidence for overexpression in a subset of human mammary tumors," PNAS, 1989, 86:9193-9197, copy made of record as reference C27 in the Information Disclosure Statement filed March 2, 2009. See Figure 3 at page 9195.

mouse is a well-known model of spontaneous breast cancer (see, e.g., page 1138, left column, first paragraph of Gyorffy et al.[4]). Information which is well known to one skilled in the art need not be disclosed in order to satisfy the written description requirement. *See Capon v. Eshhar*, 418 F.3d at 1360-1361; *Falkner vs. Inglis*, 448 F.3d at 1368.

For at least these reasons, Applicant submits that the amended claims comply with the written description requirement, and withdrawal of this rejection is respectfully requested.

II. THE CLAIM REJECTIONS UNDER 35 U.S.C. § 102(b) SHOULD BE WITHDRAWN

Claims 4, 6, 9-14, 44 and 45 are rejected under 35 U.S.C. § 102(b) ("Section 102(b)") as allegedly being anticipated by WO 98/02540 to Fizpatrick et al. ("Fizpatrick et al."). Specifically, the Examiner alleges that "Fizpatrick et al teach using an ErbB-3 protein that comprises the N-terminal 636 amino acids...which necessarily comprises at least amino acid residues 24-81 of SEQ ID NO:14 of the instant application" (see Office Action, page 13, lines 4-8).

As discussed above, claim 4 has been amended to clarify that the ErbB-3 protein is not the entire extracellular domain of ErbB-3, but is a fragment of the extracellular domain of ErbB-3 that comprises (a) the amino acid sequence set forth in SEQ ID NO: 3; or (b) amino acid residues 24-81 of the amino acid sequence set forth in SEQ ID NO:14; or (c) amino acid residues 2-139 of the amino acid sequence set forth in SEQ ID NO:16.

At most, Fizpatrick et al. discloses an ErbB-3 protein that comprises the entire extracellular domain of ErbB-3. However, Fizpatrick et al. does not disclose or teach any fragment of the extracellular domain of ErbB-3, much less disclose or teach any fragment of the extracellular domain of ErbB-3 that comprises any of the recited sequences (i.e., SEQ ID NO:3, or amino acid residues 24-81 of SEQ ID NO:14, or amino acid residues 2-139 of SEQ ID NO:16).

Thus, Fizpatrick et al. does not anticipate amended claim 4 and its dependent claims 6, 9-14, 44, and 45. Withdrawal of the Section 102(b) rejections is respectfully requested.

[4] Gyorffy et al., "Adenoviral vector expressing murine angiostatin inhibits a model of breast cancer metastatic growth in the lungs of mice," Am J Pathol. 2001, 159:1137-1147, copy made of record as reference C44 in the Supplemental Information Disclosure Statement submitted concurrently herewith.

CONCLUSION

Applicant respectfully requests entry of the amendments and remarks made herein into the file history of the present application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date: March 5, 2010

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